

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 99473 WO	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP00/03747	International filing date (day/month/year) 25/04/2000	Priority date (day/month/year) 29/04/1999	
International Patent Classification (IPC) or national classification and IPC A61K31/58			
Applicant AKZO NOBEL N.V.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 			

Date of submission of the demand 28/11/2000	Date of completion of this report 31.08.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Giacobbe, S Telephone No. +49 89 2399 8463



INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

International application No. PCT/EP00/03747

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-9 as originally filed

Claims, No.:

1-9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

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(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6: Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
 - the entire international application.
 - claims Nos. 8, 9 (IA only).

because:

- the said international application, or the said claims Nos. 8, 9 (IA only) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
 - the written form has not been furnished or does not comply with the standard.
 - the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1,2,4,5,7-9
 No: Claims 3,6

Inventive step (IS) Yes: Claims
 No: Claims 1,2,4,5,7-9

Industrial applicability (IA) Yes: Claims 1-7,9

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No: Claims 8 (see Separate Sheet)

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/03747

1. Section III

Claim 8 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT). However, although not required under the provisions of the PCT, an opinion will be given with respect to novelty and inventive step.

2. Section V

2.1 Cited Documents

2.1a The following documents (D) are referred to in this Report:

- D1: WO 94 04156 A (AKZO N.V.) 3 March 1994
- D2: WO 93 21927 A (MEDICAL COLLEGE OF HAMPTON ROADS) 11 November 1993
- D3: WO 97 49407 A (AKZO NOBEL N.V.) 31 December 1997
- D4: SCHOONEN W.G.E. ET AL: 'Human progesterone receptor A and B isoforms in CHO cells. II. Comparison of binding, transactivation and EDD50 values of several synthetic (anti)progestagens in vitro in CHO and MCF-7 cells and in vivo in rabbits and rats' J. STEROID BIOCHEM. MOL. BIOL., vol. 64(3), 1998, pages 157-170

Unless otherwise indicated reference is made to the passages cited in the Search Report.

2.1b The content of the cited documents is the following:

- i) document D1 discloses the combination of a multi-phase progestin preparation and preferentially 14 sequential dosage units of a anti-progestin compound, e.g. Org 33245, for use in contraception. Decreased bleeding is mentioned as additional advantage (cf. p. 2, l. 33);
- ii) document D2 discloses regimens of progestin-only preparations and intermittent anti-progestin, e.g. once every 30 days. Org 31710 is explicitly mentioned as a preferred anti-progestin. Decreased bleeding is mentioned as additional advantage (cf. p. 3, ll. 13-17);
- iii) document D3 discloses regimens of progestin-only preparations and

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intermittent anti-progestin, e.g. twice every 30 days for use as contraceptive and/or for HRT. Org 31710 is explicitly mentioned as a preferred anti-progestin. Decreased bleeding is mentioned as additional advantage (cf. p. 2, ll. 13-16);

iv) in document D4 the anti-progestinic activity of Org 33245 is compared to that of Org 31710, *in vitro* and *in vivo*. It is shown that the former is more active than the latter.

2.2 Art 33(2) PCT (Novelty)

The subject-matter of present claims 3 and 6 does not meet the requirements of Art 33(2) PCT since it is anticipated by the disclosure of document D1.

n.b. Contraception is not considered as a method of treatment of the body by therapy, since pregnancy is not a disease. Therefore a claim formulated following the Swiss format (i.e. claims 1-4) are considered as directed to a non-medical use of the named compositions and therefore as not-novel if the compositions themselves are known. Claim 7 (and 9, as far as it refers to 7) are considered as non-medical method claims.

2.3 Art 33(3) PCT (Inventive step)

The subject-matter of present claims 1, 2, 4, 5 and 7-9 does not meet the requirements of Art 33(3) PCT.

Documents D2 and D3 constitute the closest prior art. The technical problem to be solved can be formulated as "how to find a contraceptive preparation alternative to that of D2 and D3". The disclosure of document D4 clearly suggests to the skilled person as a possible solution the use Org 33245 instead of Org 31710, thereby rendering the subject-matter of the aforementioned claims obvious.

2.4 Art 33(4) PCT (Industrial applicability)

As stated above, no opinion is given on the question of whether present claim 8 is industrially applicable since its patentability is *inter alia* dependent upon its formulation as well as upon national and regional laws and no unifying criteria is provided in this field by the PCT.

3. Section VIII

The term "intermittent" in claims 5 and 7-9 is not clear.

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

Top

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in its capacity as elected Office

Date of mailing (day/month/year) 09 January 2001 (09.01.01)	ETATS-UNIS D'AMERIQUE in its capacity as elected Office
International application No. PCT/EP00/03747	Applicant's or agent's file reference 99473 WO
International filing date (day/month/year) 25 April 2000 (25.04.00)	Priority date (day/month/year) 29 April 1999 (29.04.99)
Applicant	
COELINGH BENNINK, Herman, Jan, Tijmen et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

28 November 2000 (28.11.00)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p>	<p>Authorized officer R. E. Stoffel</p>
<p>Facsimile No.: (41-22) 740.14.35</p>	<p>Telephone No.: (41-22) 338.83.38</p>

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(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
9 November 2000 (09.11.2000)

PCT

(10) International Publication Number
WO 00/66129 A3(51) International Patent Classification⁷: A61K 31/58

(NL). SCHOONEN, Wilhelmus, Gerardus, Eduardus, Joseph [NL/NL]; Parklaan 16, NL-5345 BV Oss (NL).

(21) International Application Number: PCT/EP00/03747

(74) Agent: KRAAK, Hajo; P.O. Box 20, NL-5340 BH Oss (NL).

(22) International Filing Date: 25 April 2000 (25.04.2000)

(81) Designated States (national): AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA.

(25) Filing Language: English

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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(71) Applicant (for all designated States except US): AKZO NOBEL N.V. [NL/NL]; Velperweg 76, NL-6824 AB Arnhem (NL).

Published:

— With international search report.

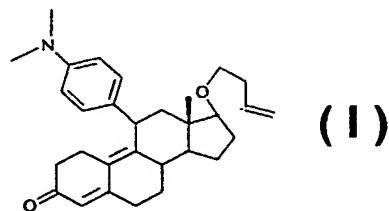
(88) Date of publication of the international search report:
19 April 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(72) Inventors; and

(75) Inventors/Applicants (for US only): COELINGH BEN-NINK, Herman, Jan, Tijmen [NL/NL]; Melvill van Carnbeelaan 38, NL-3971 BE Driebergen (NL). DECKERS, Godefridus, Hermanus, Johanna [NL/NL]; van Limburg Stirumstraat 34, NL-5344 HW Oss (NL). DOLS, Paul, Peter, Marie, Antonius [NL/NL]; Ringelenburg 1, NL-5346 VR Oss (NL). ORLEMANS, Everardus, Otto, Maria [NL/NL]; Wolvespoor 12, NL-5343 XM Oss

(54) Title: USE OF ANTI PROGESTAGENS IN COMBINED THERAPY



WO 00/66129 A3

(57) Abstract: It has been found that the compound satisfying the structural formula (I) given below has a surprisingly good suitability for being administered intermittently. This particular compound therewith has the highly advantageous property that it can be used in the specific medical application of combined therapy with progestagen-only preparations.

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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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INTERNATIONAL SEARCH REPORT

Application No
/EP 00/03747A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/58

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 04156 A (AKZO N.V.) 3 March 1994 (1994-03-03) page 3, line 20-22; claims 1,4,8 page 2, line 9,10 page 3, line 36-38	6,7
A	WO 93 21927 A (MEDICAL COLLEGE OF HAMPTON ROADS) 11 November 1993 (1993-11-11) cited in the application page 4, line 26-34; claims 1-5,9-16,20,21 page 9, line 32-35 page 10, line 12-17 page 7, line 20-31	1,2,4,5
Y		1-9

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

20 December 2000

Date of mailing of the international search report

29/12/2000

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Authorized officer

Kanbier, D

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INTERNATIONAL SEARCH REPORT

Application No

EP 00/03747

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97 49407 A (AKZO NOBEL N.V.) 31 December 1997 (1997-12-31) cited in the application page 2, line 18-28; claims 1-4,9,10 page 4, line 5-9	1,2,4-7, 9
Y	SCHOONEN W.G.E. ET AL: "Human progesterone receptor A and B isoforms in CHO cells. II. Comparison of binding, transactivation and EDD50 values of several synthetic (anti)progestagens in vitro in CHO and MCF-7 cells and in vivo in rabbits and rats" JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, vol. 64, no. 3, 1998, pages 157-170, XP002124156 United Kingdom page 164, right-hand column -page 165 page 167, right-hand column, line 1-4	1,3,5-8
A	WO 93 17686 A (SCHERING AG) 16 September 1993 (1993-09-16) page 4, line 14-16 page 5, line 28-36 page 7, line 3-7 page 10, line 19-23 page 9, line 31 -page 10, line 9	1,2,4-9
A	EP 0 549 041 A (AKZO N.V.) 30 June 1993 (1993-06-30) cited in the application claim 6; example 1	1,3,5-8

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Inten. I Application No.
EP 00/03747

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9404156	A 03-03-1994	AU 4708993	A	15-03-1994
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INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte

Application No

EP 00/03747

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